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## Deaf Scientists Contribute to Lab Success

**P**eter Blumberg, Ph.D., reveals one secret to staffing his laboratory with top researchers: "We have better-quality applicants here at CCR than we otherwise would because we take advantage of a pool of highly talented people who somebody else has not scooped up."

The CCR is home to the largest concentration of Deaf scientists in one NIH laboratory, due in large part to Dr. Blumberg. Five years ago, as one aspect of his recruiting efforts, Dr. Blumberg decided to look for capable Deaf scientists. Very happy with the results, he has continued to network in search of more such scientists for his Molecular Mechanisms of Tumor Promotion Section; he currently employs three.

About five years ago, Dr. Blumberg hired a Deaf woman for a job at his horse farm near Frederick, Maryland. He began to learn sign language to help their communication. Later, while attending a large internal NIH event, he noticed that there was no interpreter. "I realized that maybe there was a gap and thought CCR/NCI ought to be in the lead," Dr. Blumberg said. "NIH is dedicated to making sure all Americans have access to training in the biological sciences. Different groups have focused on different things as they try and make that policy a reality."

Dr. Blumberg recognized that Washington, DC's Gallaudet University, the world's only university where all programs and services are designed specifically for Deaf and hard-of-hearing students, represents a special opportunity for the NIH. Each time he needs candidates for an opening, he visits the university or e-mails some of the faculty. One

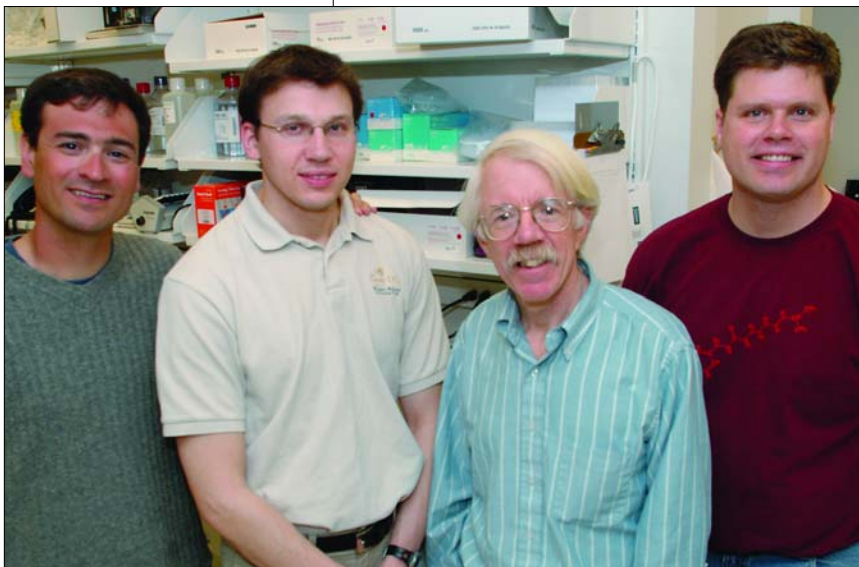
of his current scientists, Derek C. Braun, Ph.D., is assistant professor of biology at Gallaudet and a valuable contact.



Larry V. Pearce, B.S., and Peter Blumberg, Ph.D., discuss the design of an experiment.

Dr. Blumberg is adamant that the Deaf scientists get no special breaks in their expected standard of work and produce an excellent number of papers. "No one gets preferential treatment," he said. "We have a research mission here at CCR, and it doesn't do anyone any good to not fit in right with the job they are doing. All the scientists in my group are very productive."

*(continued on page 2)*



Derek C. Braun, Ph.D.,  
Vladimir Pavlyukovets, B.A.,  
Peter Blumberg, Ph.D., and  
Larry V. Pearce, B.S.

*"When I arrived at  
the lab, I felt quite  
a bond with Peter.  
I knew he was trying  
to include me,"  
said Mr. Pearce.*

The scientists and Dr. Blumberg communicate using sign language, and in some cases reading lips and voicing; when they need to communicate with non-signing individuals or with larger groups, such as at lab meetings or seminars, the scientists book one of the NIH's pool of nine sign-language interpreters.

The Deaf scientists in Dr. Blumberg's lab are Gallaudet's Dr. Braun, who volunteers 3 days a week; technician Larry V. Pearce, B.S.; and post-baccalaureate student Vladimir Pavlyukovets, B.A.

Dr. Braun said his experience at the CCR working in cell signaling has been "wonderful," partially because Dr. Blumberg is an "outstanding boss, with a new idea every week," and the NIH provides a ready supply of interpreters.

Dr. Braun, who lost his hearing at age 3 due to an antibiotic course for an illness, said deafness is no longer an obstacle to his career, although Deaf students sometimes face problems being accepted into graduate school. Nonetheless, he said Deaf people "are very underrepresented in the world of science. It would be nice if more NIH institutes had a similar program to CCR's."

Mr. Pearce and Mr. Pavlyukovets, both of whom attended Gallaudet, relish their opportunities in Dr. Blumberg's lab. Mr. Pearce, whose deafness was caused by spinal meningitis when he was 18 months old, said, "When I arrived at the lab, I felt quite a bond with Peter. I knew he was trying to include me." Mr. Pearce works on cell

signaling and pain pathways and has published 14 papers since joining the lab in 2000.

Mr. Pavlyukovets joined the lab in August 2003. Recently, he was accepted into the Johns Hopkins University graduate program in Biotechnology, where his study will focus on molecular targets and drug discovery technologies. This new program is a joint initiative between Johns Hopkins and the CCR/NCI. Born deaf, Mr. Pavlyukovets said he does not have the advantage of being able to lip read or voice well. But he now has four languages under his belt: Russian, Russian Sign Language, English, and American Sign Language.

Reflecting on the relative rarity of Deaf employees in science, Dr. Blumberg said, "Folks who don't have any experience dealing with Deaf scientists may be worried that it's a big deal to accommodate such people and that it takes up more time. But the same people may hire scientists from other countries whose English is quite limited. Employees who are ineffective take up a lot more of your time than those who are effective."

Dr. Blumberg said having Deaf scientists on board has educated not only people in his lab, who see that hearing has nothing to do with the ability of scientists to do their jobs, but it has been an eye-opener for foreign fellows from countries where Deaf people may be hidden away rather than embraced by society.

Dr. Blumberg recalled that, while a graduate student at Harvard University 34 years ago, he heard about the strategy of a Tufts University Department of Microbiology chairman for recruiting outstanding graduate students to his department. His tactic was to hire top candidates who were typically rejected by other prestigious institutions in Boston. His secret: they were women. ■

Note: The word "Deaf" is capitalized as a reference to members of the Deaf community and Deaf culture.

## Postdocs “Energized” by Unique Retreat

In blustery March this year, more than 400 NCI postdoctoral and research fellows hung up their lab coats and left town for a CCR-sponsored two-and-a-half-day retreat. Far from the NIH campus, in a large hotel in Williamsburg, Virginia, they attended scientific presentations and career workshops by day, then networked and toured scientific poster displays by night.

The annual CCR Fellows and Young Investigators (FYI) Retreat is unique within the NIH, and it's among the reasons NCI was recently voted the fourth best workplace in the nation for postdocs.\* At the retreat, high-caliber speakers cover cutting-edge science, workshops focus on career advancement, fellows and young investigators make oral or poster presentations on their research, and lunches function as mentoring opportunities. Social time after the day's work promotes networking, which is key for building contacts that lead to collaborative science projects down the road.

Holding retreats well away from the NIH campus allows the postdocs and research fellows to release laboratory stress and give full attention to the retreat's content. In the lab, scientists are often microscopically focused on their work, but at these retreats they can ponder the picture behind their projects—visualize collaborative medicine and curing cancer. “If we hold retreats close enough to NIH, it is harder to detach their focus from their day-to-day work,” said Jonathan Wiest, Ph.D., the CCR's associate director of training and education, of the postdocs and fellows. “We all have about six jobs that we are doing that demand our attention.” The retreat allows a much-needed opportunity to learn without the normal distractions.

On the networking side, the retreat provided the structure for fellows to get to know each other better and to talk to some of the big names in various scientific fields. There was a meet-and-greet session, mentoring lunches which sat fellows at a 10-person lunch table with a senior scientist, and lounges where everyone could relax at the end of the day. “The social side was great,” said Kwang Suh, Ph.D., a postdoc who helped organize the retreat. “This was the first time where just the fellows from our institute got together to see each other's work. Sometimes, we just meet in elevators or at small seminars given in the lab. You know faces but never have the chance to strike up a conversation.”

And this familiarity can help build fruitful working relationships. “This is an opportunity to interact on a scientific level with friends down the hall,” Dr. Wiest said. “It is important for fellows to build strong collaborations at this point in their careers. People they network with now are people they'll be collaborating with their entire career.”

Unusually, the FYI Retreat is organized by postdocs themselves, specifically members of the FYI steering committee. This year's movers and shakers included Cem Elbi, M.D., Ph.D., Dr. Suh, and Melissa Maderia, Ph.D. The organizers typically solicit ideas for speakers and workshops, then ask all postdocs to vote. They set the agenda, help with publicity, score abstracts, and oversee the retreat itself. This year, as well as dealing with the largest number of attendees yet, the organizers managed 267 abstracts, 5 keynote speakers, and 5 workshops.

Helping run such an event takes a lot of time and effort but builds confidence and teaches the organizers new skills. Dr. Maderia said her

*“People they network with now are people they'll be collaborating with their entire career,” said Dr. Wiest.*



Eiman Aleem, Ph.D., a postdoc in the Cell Cycle Regulation Section of the Mouse Cancer Genetics Program, explains her work with genetically altered mice. Dr. Aleem won an honorable mention for this poster.

\*Postdocs Pick Institutions that Build Community, *The Scientist*, 17(3), Feb. 10, 2003.



Sachindra Patil, Ph.D., from the Laboratory of Medicinal Chemistry, discusses his poster on the design of anti-HIV drugs with a fellow postdoc at the FYI Retreat in Williamsburg, Virginia.

newfound understanding of all that goes into planning such an event will be invaluable when she eventually becomes a professor at a small college—a role that would likely entail conference planning.

Before the retreat, more than half of the attendees submitted abstracts of their work. These were judged by the FYI

steering committee, with the top 5 abstracts in each of 8 categories selected for oral presentations and another 40 for poster presentations. More judging occurred during the retreat, with 4 oral presenters and 4 poster presenters receiving \$1,000 travel awards to attend any U.S.-based scientific meeting.

Postdocs and fellows created colorful 4-foot by 6-foot posters that illustrated their work or they gave 10-minute talks, then answered questions for 5 minutes. Although many researchers often present their data to teammates at small gatherings, the retreat was a more challenging forum. “The more often you present your work, the better you get at doing it,” Dr. Wiest said. “The more you have to field questions, the more you may think about things in a different way.”

Another notable part of the Williamsburg retreat was an open-ended session arranged for CCR scientists to discuss issues and raise questions with J. Carl Barrett, Ph.D., director of the CCR. “It was very, very good for the fellows to interact directly with their director,” Dr. Elbi said. “There was valuable feedback from both sides.”

Dr. Suh said feedback from the retreat showed that “it was very educational for a lot of postdoc fellows as well as postbacs [postbaccalaureate students]. I could just see fellows being energized when they were here.” He added that he hopes even more CCR fellows and their principal investigators will recognize the retreat’s benefit so more CCR postdocs and fellows will attend.

Claudina Stevenson, Ph.D., of the Dana-Farber Cancer Institute (a teaching affiliate of Harvard Medical School), was so impressed with the retreat that she is launching a similar one back home. Dr. Stevenson, a former CCR postdoctoral fellow who helped plan past FYI Retreats, said, “I am positive that active collaborations have formed as a result of people talking to each other at the events.” ■

*Although many researchers present their data to teammates at small gatherings, the retreat was a more challenging forum.*



## RETREAT HIGHLIGHTS

### Keynote Presentations at the 2004 FYI Retreat

- Stephen J. Lippard, Ph.D., Massachusetts Institute of Technology (MIT), “Platinum Anticancer Drug Research in the Hands of a Chemist.”
- Robert A. Weinberg, Ph.D., Whitehead Institute of Biomedical Research, MIT, “Mechanisms Governing the Formation of Human Cancers.”
- Shiv Grewal, Ph.D., National Cancer Institute, “RNAi-Mediated Epigenetic Control of the Genome.”
- Stanley B. Prusiner, M.D., University of California, San Francisco, 1997 Nobel Laureate in Medicine, “The Clarion Call of the Mad Cow.”
- J. Carl Barrett, Ph.D., CCR director, NCI, “Mechanisms of Cancer Progression.”



### Workshop Topics

- Negotiating skills for the job seeker.
- Team science.
- Being a professor: What you thought you knew.
- Time mastery (management skills).
- Grant writing.

Dr. Barrett delivers a keynote speech to the postdocs.



## Teamwork Yields Successful Research

The days when a scientist would study one or two genes for an entire career are gone. Now, in high-throughput experiments, bench scientists can simultaneously study thousands or tens of thousands of genes in only hours and complete the analysis and interpretation in a matter of months. To deal with this enormous jump in scale, CCR geneticists and cancer researchers increasingly collaborate with intramural and extramural investigators who specialize in such diverse fields as molecular biology, pharmacology, bioinformatics, biostatistics, and computer science.

At NCI, Faculties make such interdisciplinary work easier. “The Faculties provide a forum through which interdisciplinary and multidisciplinary research teams can be formed,” said J. Carl Barrett, Ph.D., director of the CCR. “These teams bring together diverse expertise that can make truly significant scientific advances that would be difficult for an investigator working alone.”

One collaborative team has already produced results—two new molecular markers that may help tell whether a metastasized cancer originated in the ovary or in the colon.

In 2002, Satoshi Nishizuka, M.D., Ph.D., a research fellow in the Laboratory of Molecular Pharmacology, initiated a multistep protocol, or plan, for finding new markers that would reveal whether a patient’s malignancy originated in the colon or ovary, a call that can be difficult to make, leading to a diagnosis of “cancer of unknown origin.” This distinction is important because it determines what type of treatment a patient receives.

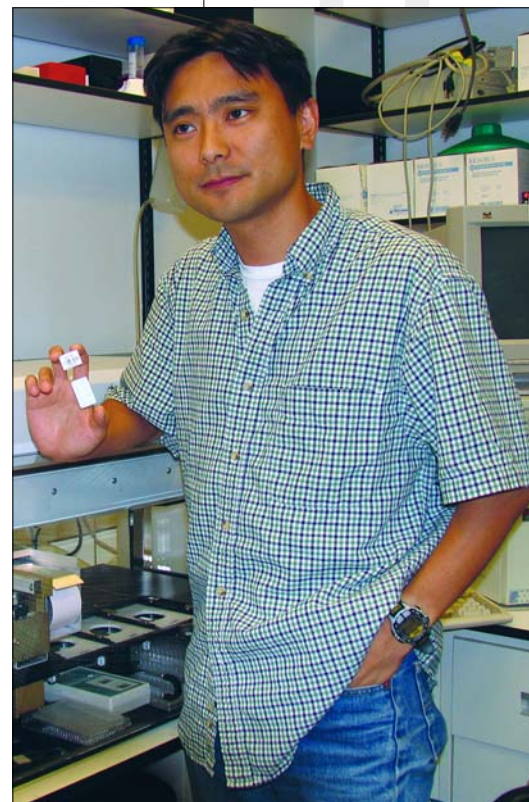
Dr. Nishizuka, along with a team of CCR researchers from the Laboratories of Molecular Pharmacology and Pathology, started their research with the “NCI 60”—the 60 human cancer cell lines NCI uses to screen for anticancer agents. They examined data from

microarray studies of these cultured cells to find genes that were expressed in colon cancers but not in ovarian, and vice versa. To see if the markers would hold up at the protein level, the researchers tested them through protein arrays developed in CCR laboratories. Finally, they needed to see if the findings held true for human tumors, so they conducted experiments on multitumor tissue arrays from the CCR’s Tissue Array Research Program, which includes samples of tumors from hundreds of patients.

Overall, the project required the researchers to work closely with biostatisticians and bioinformaticists from the Bioinformatics, Biostatistics, and Computational Biology (BBCB) Faculty, as well as with computer scientists who developed software to analyze the genomic and proteomic data from the tissue arrays.

The Faculties, established in 2002, are frameworks that enhance communication and collaboration across the usual lines that divide laboratories, branches, and divisions. By supporting molecular pathologists, pharmacologists, and biostatisticians working in concert, the BBCB Faculty’s involvement was key to bridging the gap between laboratories, departments, and specialties by encouraging researchers with different disciplines to take up different parts of the project.

“Each of those subcultures has its own language, own methods, own points of focus, and own journals, so it takes flexibility and openness as well as a willingness to sacrifice a certain amount of time and effort if communication is to be effected,” said John N. Weinstein, M.D.,



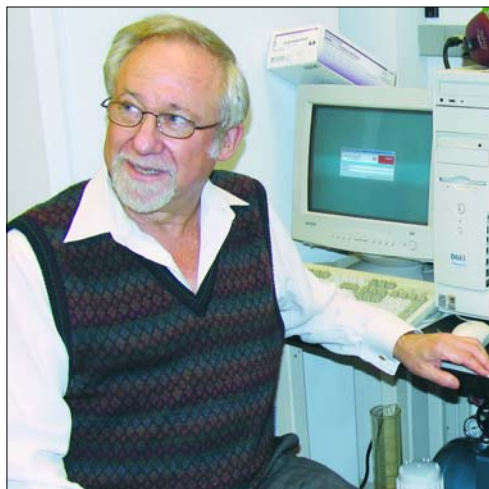
Satoshi Nishizuka, M.D., Ph.D., displays a protein microarray in the lab.

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*"The Faculties provide a forum through which interdisciplinary and multidisciplinary research teams can be formed," said J. Carl Barrett, Ph.D., director of the CCR.*

Ph.D., head of the BBCB Faculty. "CCR's faculties help provide that environment."

The protocol identified two potential molecular markers: villin for colon cancer cells and moesin for ovarian cancer cells. "The results held up well, and we produced very good statistics for distinguishing colon from ovarian cancer" using the new biomarkers, said Dr. Weinstein. He cautioned, however, that such findings must surmount many hurdles before being accepted for clinical use. The multistep process developed by the group also may be helpful in finding additional markers for cancer diagnosis, prognosis, and therapy.



John Weinstein, M.D., Ph.D.

Dr. Weinstein said the CCR's faculty framework "increases the power and the range" of those involved in multidisciplinary or multistep studies, such as the ovarian and colon cancer marker identification. Along with facilitating research collaborations, the BBCB faculty developed a concept proposal to organize bioinformatics in the intramural program, holds seminars and retreats, and otherwise facilitates group discussions of cancer problems and possible steps to help solve them. ■

— Cathy Kristiansen



## A TALENTED TEAM

Many individuals and diverse disciplines worked together to develop the new biomarkers, as shown in the publication byline:

### **Diagnostic Markers that Distinguish Colon and Ovarian Adenocarcinomas: Identification by Genomic, Proteomic, and Tissue Array Profiling**

*Cancer Research* 63, September 1, 2003, pages 5243–5250.

#### **Intramural Participants from the National Cancer Institute, NIH**

Genomics and Bioinformatics Group, Laboratory of Molecular Pharmacology: Satoshi Nishizuka, Fuad G. Gwadry, Jes Alexander, Sylvia M. Major, Uwe Scherf, William C. Reinhold, Mark Waltham, Kimberly J. Bussey, Sohyoung Kim, Samir Lababidi, Jae K. Lee, and John N. Weinstein.

Laboratory of Pathology: Sing-Tsung Chen, Lu Charboneau, Stefania Pittaluga, Lance A. Liotta, Stephen M. Hewitt, and Mark Raffeld.

Office of the Associate Director, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis: Edward A. Sausville.

Analytical Biostatistics Section, Mathematical and Statistical Computing Laboratory, Center for Information Technology: Lynn Young and Peter J. Munson.

#### **Extramural Participants**

SAIC-Frederick, Inc.: Dominic A. Scudiero of the National Cancer Institute at Frederick.

FDA: Emmanuel F. Petricoin III of the Tissue Proteomics Unit, Division of Therapeutic Proteins, Center for Biological Evaluation and Research.

## Researchers Lay Groundwork for New Vaccines

As scientists worldwide hunted for a way to stop a killer virus, two CCR researchers and their laboratory team made a remarkable discovery that threw open the doors to success. The subject of the hunt was the human papillomavirus (HPV), agent provocateur in more than 99% of cervical cancers. The discovery was a particular property of the virus that scientists could use against it in a vaccine.



CCR researchers Douglas R. Lowy, M.D., and John T. Schiller, Ph.D., and other scientists were pursuing two of the most problematic HPV types among more than 100 now identified, HPV16 and HPV18. The cancer-implicated viruses show no symptoms and typically lurk in the body for about 20 years before causing pre-cancerous changes in cervical cells. Cervical cancer is the second most deadly cancer among women around the world. Regular screening and early treatment in the United States make it 15th most deadly here, but it strikes 10,520 U.S. women each year and kills nearly 4,000.

At the time of their big discovery in 1992, Dr. Lowy and Dr. Schiller were already experienced at investigating animal and human papillomaviruses. “Most of our research on the papillomavirus has been fundamental,” Dr. Lowy said, “trying to understand the biology of the virus, answering how the virus operates, what are the functions of its different genes, and how it transforms cells.”

As they plugged away in their Laboratory of Cellular Oncology at CCR, Dr. Lowy, Dr. Schiller, and their team observed that expressing one specific viral protein created empty particles that resembled the virus. Antibodies attacked these particles, thwarting the authentic virus’ attempts to infect cultured cells. Most vaccines work by using a harmless dose of a weakened virus or of inactivated virus particles

to teach the immune system about the virus. “The results were exciting because they suggested the empty virus-like particles might lead to an effective HPV vaccine,” Dr. Lowy said. After the team’s discovery, scientists tackling HPV who generally believed particles could not be made turned on their heels to race down the particle track.

Then another hurdle appeared: scientists couldn’t get HPV16 to make particles efficiently. Dr. Lowy, Dr. Schiller, and their team made a second key discovery—the HPV16 version that scientists were using, derived from a tumor, had mutated. By culling another, pre-cancer version of the virus, the scientists overcame this hurdle and produced abundant quantities of HPV16 particles.

But would the vaccine, which had been tested in cows, rabbits, and dogs, work in humans? The CCR researchers showed that women’s immune systems mirrored the successful immune responses in model animals. These results laid the groundwork for the testing of two prototype vaccines that, in early clinical trials, appeared totally effective in preventing the targeted HPV infections, with negligible side effects.

One vaccine is in the final testing stages with the guidance of colleagues at the NCI’s Division of Cancer Epidemiology and Genetics, the

John Schiller, Ph.D., and Douglas Lowy, M.D.

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*The CCR researchers showed that women's immune systems mirrored the successful immune responses in model animals.*

other component of NCI's intramural research program. They are running an independent Phase III clinical trial in Costa Rica involving 15,000 women. The vaccine, developed by pharmaceutical companies GlaxoSmithKline and MedImmune, Inc., targets HPV16 and HPV18. Another pharmaceutical company, Merck & Co., Inc., is conducting Phase III trials of its own vaccine against the same two HPV types. (Merck's vaccine also targets HPV6 and HPV11, which cause genital warts but do not cause cancer.)

Dr. Lowy has high hopes that a version of the vaccine can come to market in less than 5 years and begin to stop the virus from infecting new people. "In terms of reducing the incidence of cancer," Dr. Lowy said, "the vaccine is likely to have a greater impact in many countries in the developing world," where millions of women lack access to the regular Pap smears that can catch HPV cancers early. "But the impact of the vaccine would take quite a long time to be felt. Between infection and incidence of cancer, there is a 20- to 30-year lag time, generally." In the United States a vaccine would reduce the worry and financial cost of treating abnormal cells and cut fatalities of women who don't get screened.

The next phase of the work is to create a pan-HPV vaccine that might be able to target all 15 cancer-causing HPVs, rather than only some of them. As part of the groundwork, CCR scientists are devising a new lab test—a "high-throughput virus neutralization assay"—that will show whether antibodies are able to prevent infection by any HPV type in cultured tissues. This test is easier to use and less expensive than earlier neutralization assays, and it covers all HPV types.

And even if the killer tries to outfox scientists by evolving into new types, Dr. Lowy said biological technology will keep pace with such tricks and develop new vaccines as needed. ■

—Cathy Kristiansen

JANUARY 2005



## HIGH-RISK RESEARCH

The research Dr. Lowy and Dr. Schiller conducted on HPV was intramurally funded, meaning that the NIH provided research funds to labs on the NIH campus without requiring that they apply in advance for grants, as happens for extramural projects—those conducted at universities, hospitals, and other research establishments around the country. Dr. Lowy said much of the team's success was due to the flexibility of the intramural system and the way it encourages its principal investigators to pursue high-risk, high-reward research. "We had the freedom to choose a risky project that would have high potential impact if it succeeded," he said.

To continue to merit such flexibility, intramural researchers need to show, retrospectively through their overall research accomplishments, that their resources have been used wisely. By contrast, the extramural grant process requires that researchers develop considerable preliminary data before they can be considered for NIH funding, making it much more project-specific than the funds provided on an intramural basis.

## CCR NETWORKS

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